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Clinical Science

Common Carotid Artery Thickness in Chronic Kidney Disease

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Key words: intima-media thickness; ultrasononography; chronic kidney disease; cardiovascular risk factors.

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Abstract

AIM: Previous studies showed that patients with chronic kidney disease (CKD) > 2 dergee had increased intima-media thickness (IMT). We evaluate the relationship between IMT and parameters for renal function.

METHODS: 130 subjects were examined – 66 with CKD, 44 without CKD, as well as 20 healthy volunteers. The first group- patients with CKD were with creatinine clearance (CrCl) over 20 ml/min and below 90 ml/min. The second group included 44 pts. with normal renal function, CrCl > 90 ml/min. All examined patients with and without CKD had hypertension. The two groups were streamed into two subgroups: with and without vascular disease. To evaluate the renal function creatinine clearance was calculated in ml/min. IMT was measured in both common carotid artery (CCA) using high resolution sonography in all examined subjects.

RESULTS: CCA IMT increased in pts. with CKD and was > 0.75 (0.76 ± 0.14 v.s contols 0.59 ± 0.10) Patients with vascular disease (VD) had higher IMT which increased significant when CKD with GFR < 90 ml/min was included (0.77 ± 0.06/0.81 ± 0.10, $p < 0.05$). Multiple regression analysis proved that renal function deterioration directly affected CCA IMT (R^2=0.208, p=0.022).

CONCLUSION: Increased IMT is presented in mild renal dysfunction. CKD –GFR< 90 ml/min could be an independent vascular risk factor.

Introduction

Chronic kidney disease (CKD) with GFR < 90 ml/min is defined as a “vasculopathic state”[1]. Cardiovascular risk in patients with CKD with imraired renal function is 10-20 times higher than in that of the general population [2]. Cardiovascular complications are major cause of morbidity and mortality in patients with CKD [1]. The intima-media thickness (IMT) of the common carotid artery (CCA) has proved to be a good marker for both the presence of early atherosclerosis and the degree of atherosclerosis of an individual [3-6]. Ultrasound measurement of (IMT) gives valuable information about the vessel status [7]. Prospective studies have shown a positive correlation between increased carotid artery IMT and the risk for myocardial infarction, stroke, and cardiovascular mortality [3-5]. Classic risk factors- age gender, hypertension duration and severity, obesity, diabetes, directly affect IMT. In contrast to the general population, for patients with CKD facing high risk of cardiovascular disease there aren’t many prospective studies on the assessment of IMT changes as well as on association of these changes with the classic and specific for CKD cardiovascular risk factors (CVRF) [8, 9]. Previous studies showed that patients with CKD with GRF < 90 ml/min had increased IMT [8, 9]. There are a few data about how impaired renal function influences carotid vascular structure [6, 10]. We evaluate the relationship between IMT and parameters for renal function deterioration.

Material and Methods

One hundred thirty (130) subjects were examined – 66 with CKD, 44 without CKD, as well as 20 healthy volunteers. The first group- patients with CKD were with creatinine clearance (CrCl) over 20 ml/min and below 90 ml/min. The second group included 44 pts. with normal renal function, CrCl > 90 ml/min. All examined patients with and without CKS had hypertension. The mean duration of hypertension was 14.45 ± 7.29 years. 20/66 pts had diabetes. 25/44 pts of the group without CKD had diabetes type 2. The two groups were streamed into two subgroups: with and without vascular disease (coronary,

peripheral vascular or brain vascular). Twenty healthy persons with normal blood pressure (12 F/ 8 M, mean age 45.8 ± 5.2, CrCl 117 ± 18 ml/min) were used as a control group for IMT measurement.

Classical CVRF: duration of arterial hypertension and diabetes, lipid metabolism as well as BMI was given in all patients. The normal BMI was up to 24. To evaluate the renal function in all examined subjects (n=130) creatinine clearance was calculated in ml/min according to the Cockcfort –Gault formula in ml/min. The normal CrCl was (> 90 <160 ml/min.)

$$\text{CrCl} = \frac{(140\text{-age}) \times \text{kg} \times 0.814 \ (\times 0.85 \text{ for female})}{\text{Serum creatinine}}$$

Table 1: Distribution of the patients into groups and subgroups.

Groups	CKD (N=66) 26M/40F 32/ 66 HAD VD**	NORMAL RENAL FUNCTION (N=44), 17M/27F 19/44 HAD VD**	HEALTHY VOLUNTIERS (N=20) 12F/8M
Age	59.9 ± 14.14	55.7 ± 15.2	45.8 ± 5.2
Serum creatinin µmol/l	232 ± 54.03	98 ± 15.11	88.7 ± 6.8
CrCl * ml/min	36.98 ± 10.55	91.11 ± 19	117 ± 18

*Cr Cl- creatinine clearance; ** VD- vascular disease- coronary artery, brain vascular disease or peripheral vascular disease.

Intima-media thickness

IMT for either common carotid artery was measured. A total of 260 IMT were examined. IMT was determined by high resolution ultrasonography-ATL Phillips in B-mode regime, using 10 MHz linear transducer as described by Kawagishi and Adaikkappan and Pignoli P [11]. The common carotid arteries were scanned in longitudinal and transversal projection. Each patient had undergone individual optimisation of the depth and gain adjustment. IMT was measured in an anterolatteral position 2 см away from the bifurcation. The given values are the average of three consecutive measurements. Normal value for IMT was considered < 0,65mm

Statistic methods

Statistical software programs (SPSS 15.0.1) were used. All data were expressed as mean ± SD. Statistical comparisons between two groups were made with a two–sample t- test. P< 0.05 was considered as statistically significant value. To study the linear relationship between CCA IMT and other variables Pearson's correlation test was used. Multivariate logistic regression analysis was performed to assess the influence of the chronic renal failure on the CCA IMT values.

Results

Significant differences in the mean values of IMT for right and left carotid artery in all examined groups were not found. This is given in Table 2. Intima-media was thickened in pts with CKD the mean value was over 0.75mm. The values in the CKD group were significantly higher than those in the healthy controls. In the latter IMT was normal (Table 2).

Table 2: Comparative analysis of IMT between patients with renal failure and healthy volunteers.

Group	CrCl ml/min	IMT* OF THE RIGHT CCA**	IMT * OF THE LEFT CCA
CKD (n=66)	36.98 ± 10.5	0.76 ± 0.10 mm	0.77 ± 0.06
HEALTHY SUBJECTS (n=20)	117 ± 18	0.59 ± 0.10 mm	0.60 ± 0.12
P	< 0.001	< 0.001	< 0.001

* IMT- intima- media thickness; **CCA- common carotid artery.

Intima-media is thickened in patients with CKD, its value being significantly higher when VD factor was added, p < 0.05. Patients with VD without CKD had increased IMT of a value that is comparable to the mean value of IMT in the pts. from the CKD group (0.77 ± 0.06/0.76 ± 0.10, p = NS) (Table 3).

Table 3: Mean values of IMT patients with and without CKD with GFR < 90 ml/min and healthy volunteers.

Group	CrCl ml/min	IMT of the right CCA	IMT of the left CCA	p
CKD (n = 66)	36.98 ±10.55	0.76 ± 0.10	0.77 ± 0.06	n.s
CKD+VD* (n = 32)	37.09 ± 9.55	0.81 ± 0.10	0.80 ± 0.06	n.s
CKDwithout VD* (n = 34)	39.29 ± 11.78	0.75 ± 0.10	0.74 ± 0.06	n.s
Without CKD (n = 44)	91.11 ± 19	0.77 ± 0.1	0.78 ± 0.06	n.s
VD without CKD (n = 19)	89 ± 11.6	0.77 ± 0.06	0.78 ± 0.09	n.s
Without CKD.without VD (n=25)	105 ± 13.37	0.70 ± 0.22	0.71 ± 0.06	n.s
Healthy controls (n = 20)	117 ± 18	0.59 ± 0.10	0.60 ± 0.12	n.s

To evaluate how important the study of IMT in the effort to precisely examine the early vessel changes in patients with CRF in predialysis stage, an analysis was carried out to fined the correlation between the IMT and parameters of renal function, age, BMI and the duration of diabetes and hypertension. These results are given in table 4. A negative moderate correlation of IMT with CrCl was proved as well as the same degree of positive correlation of IMT with duration of CKD, hypertension, diabetes and age.

Table 4: Correlation of IMT with renal function, duration of renal disease, hypertension and diabetes, BMI and age.

	PARAMETERS	CREATININE	CRCL	HYPERTENSION DURATION	DIABETS DURATION	CKD DURATION	BMI	AGE
Corr.coef.	IMT – right CCA	0.095	-0.303	0.394	0.343	0.324	0.032	0.351
p	p	0.488	0.003	0.023	0.045	0.006	0.814	0.062
N	N	56	56	100	45	56	100	100
Corr.coef	IMT- left CCA	0.108	-0.312	0.385	0.349	0.316	0.029	0.358
p	p	0.428	0.004	0.033	0.021	0.003	0.831	0.04
N	N	56	56	100	45	56	100	100

The regression analysis carried out proved that there was a relation between IMT and creatinine clearance which can be described by a linear model

($p = 0.022$, $R^2 = 0.208$) with the following parameters:

$$IMT = 1.546 – 0.007\ CrCl,$$

where IMT is intima-media thickness, and CrCl is creatinine clearance.

When CrCl decreases by 1 ml/min, IMT increases by 0.005 mm.

What was most important to define IMT and became the result of regression analysis was: VD presence, LDL and total cholesterol levels and CKD presence. The regression model showed that (R^2 = 0.136, p = 0.005), an increase of age with 1 year led to an IMT increase with 0.002. VD presence led to an IMT increase with 0.037.

$$IMT = 0.635 + 0.001\ Age + 0.057ChrKI,$$

where IMT is intima-media thickness, age - age, a ChrKI is CRF.

CKD was a factor that had a separate and borderline influence with the intima-media thickness formation. Results were summarized in Table 5.

Table 5: Multiple regression analysis of CCA IMT.

	NONSTANDART COEF.		STANDART COEF.	P
	B	Std. Error	Beta	
SECOND STEP				
Constanta	0.598	0.079		<0.001
Total cholesterol	0.050	0.027	0.7148	0.054
LDL cholesterol	-0.018	0.016	-0.239	0.286
CKD	0.013	0.031	0.057	0.675
Diabetes duration	0.023	0.025	0.111	0.369
Age	0.001	0.001	0.172	0.200
Hypertension duration	0.006	0.003	0.401	0.027
VD	0.070	0.028	0.351	0.013
LAST STEP				
Constanta	0.635	0.049		<0.001
Age	0.001	0.001	0.191	0.090
Vascular disease	0.057	0.022	0.286	0.012
Total cholesterol	0.021	0.011	0.303	0.054
Hypertension duration	0.005	0.002	0.353	0.041

Discussion

IMT, measured by B-image technology, is a morphological parameter and represents the histological verified intima-media segment of the vascular wall [11]. IMT in the CCA is a marker for the degree of arteriosclerosis [6, 12]. The data from the big multicenter studies VHAS (Verapamil in Hypertension and Atherosclerosis Study) и ELSA (European Lacidipine Study of Atherosclerosis) showed high frequency of CCA structural changes that had been proved by intima-media thickness measurement [13, 14]. Our results were found to be similar. In less than 30% of the pts with CKD IMT was found to be normal. This percentage in pts. with normal renal function was 35. The number of patient with proven VD in both groups was similar. This can be used to prove that CKD was a factor for vascular damage, proved also by the results from the regression analysis. A great number of epidemiological studies in general population proved the relationship between IMT and age, hypertension and diabetes duration and hyperlipidemia [3, 7]. Such correlation has been proved in our patients with CKD. The lower correlation between IMT and hypertension and diabetes duration in our pts. with CKD can be explained with the high heterogenecity of these factors and good correction of hypertension and diabetes in all examined patients.

A lot of data about the correlation between IMT and renal function have been published [15-17]. Some of them showed that in CKD patients the correction of classic cardiovascular risk factors did not reduce the thickened intima-media but the correction of classic cardiovascular risk factors in patients with normal renal function reduced the thickened intima-media.. Thus is the thesis confirmed that under the conditions of impaired renal function vascular risk factors traditional and specific for CKD act together. CKD is a complex of vasculopathic factors [18]. Our results confirmed negative a correlation between IMT and renal function assessed by CrCl as well as a positive relation between IMT and CKD duration. Similar results were published by Leoncini and coauthors. They proved that the mean IMT value in pts. with CRF was 0.79mm, which was significantly higher than that in the healthy controls (0.65 mm) with normal renal function. The role of age, hypertension duration as predictors for intima-media thickening was proved by their regression analysis. Along with that the authors pointed out that the risk for carotid atherosclerosis grew with 43% per each decrease of CrCl with 10 ml/min [19]. K.H. Rahn published similar results [8].

VD presence affected intima-media thickness independently. The examined patients with VD had thickened intima- media no matter whether they had or had not CKD. The fact that the IMT became

significantly higher in the presence of CKD with GFR < 90 ml/min is one more proof that impaired renal function is a vascular damage factor. Staneva and coauthors examined patients with normal renal function with and without coronary artery disease and came to the conclusion that the patients with coronary artery disease had significantly higher IMT which is connected with the gravity of the ischemic disease [20].

Chronic kidney disease patients with impaired renal function are people of the highest cardiovascular risk that is commensurable with the risk in diabetic patients and those who have suffered from myocardial infarction. In recent years work has been carried on to early identify the cardiovascular risk and the early vessels damage markers in high risk patients. IMT measurement in patients with CKD is a strongly-informative method for proving early vascular changes and for determining the patients with high cardiovascular risk. It is recommendable for that method to be regularly applied in the everyday practice of the nephrologists.

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